Role of the Forebrain Cholinergic Projection System in Performance in the Radial-Arm Maze in Memory-Impaired Rats.

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Impairments in performance in the radial-arm maze (involving deficits in learning, memory and/or attention) were produced in rats by one of two means: chronic administration of alcohol for 6 months, or excitotoxic lesions of the cholinergic projection nuclei to the neocortex and hippocampus. After both kinds of intervention, the animals showed profound and enduring deficits in 4 different components of memory tested in the task: reference and working spatial memory, and reference and working cue memory. Transplants of foetal cholinergic-rich brain tissue, in a cell suspension, placed into neocortex and/or hippocampus substantially reversed deficits in all 4 memory components over a time course of approximately 7-13 weeks after transplantation. Transplants of cholinergic-poor brain tissue were without effect. Both alcohol-treated and lesioned animals showed significantly reduced cortical and hippocampal levels of choline acetyltransferase (ChAT) activity. However, in rats with cholinergic-rich, but not cholinergic-poor transplants, cortical and/or hippocampal ChAT activity was elevated to control level, commensurate with site of transplant. The rats were tested prior to transplantation to determine their reactions to acute systemic administration of a range of compounds, including muscarinic and nicotinic agonists and antagonists. Both the alcohol-treated and lesioned animals showed increased sensitivity to both the beneficial effects on cognitive performance of cholinergic agonists, and the deleterious effects of cholinergic antagonists. Both muscarinic and nicotinic agents were effective. Nicotine was particularly effective in improving spatial working memory in lesioned rats. However, in lesioned rats tested after transplantation with cholinergic-rich tissue, this compound had the surprising effect of making performance in the radial-arm maze worse, although it continued to improve performance in sham-transplanted animals and in animals that had received cholinergic-poor transplants.

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